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CD4<sup>+</sup> T cells are required to combat various intestinal microbes, yet little is known about the activation of such pathogen-specific cells in vivo. We describe here an adoptive transfer system that enables visualization of Salmonella-specific CD4<sup>+</sup> T cells as they respond to an oral infection. These naïve cells reside in all lymphoid tissues but undergo clonal expansion and follicular migration exclusively within Gut-Associated Lymphoid Tissue (GALT) after infection. Surprisingly, T cell activation was not observed in the spleen of infected mice, despite the presence of bacteria and antigen-specific CD4<sup>+</sup> T cells in the same anatomical location. In addition, Salmonella-specific CD4<sup>+</sup> T cells activated in GALT did not migrate to the liver, the primary non-lymphoid site of bacterial replication. Therefore, the CD4<sup>+</sup> T cell response to Salmonella is restricted to the local mucosal environment despite the systemic nature of this infection.